Patent Application
Attorney Docket No. RC9576A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: BRONK, ET AL.

Examiner: PESELEV, E.

APPLICATION NO.: 09/424,104

Group Art Unit: 1623

FILING DATE: NOVEMBER 18, 1999

TITLE: 4"-SUBSTITUTED-9-DEOXO-9A-AZA-9A-HOMOERYTHROMYCIN A DERIVATIVES

Assistant Commissioner for Patents

Box AF

Washington, D.C. 20231

AFTER FINAL

Sir:

RESPONSE UNDER 37 CFR 1.116

This is in response to the final Office action dated January 8, 2001, rejecting claims 1-2, 14-20 and 22-28 and objecting to claims 3-13 and 21 (which would be allowable if re-written in independent form). Pursuant to a Petition for Extension of Time for two (2) months, enclosed herewith, a response is due June 8, 2001.

This response and the remarks herein are believed to support the patentability of all of the claims of the present application, such that they are presently in form for allowance, or alternatively, in form for appeal. The Examiner is respectfully requested to reconsider the final Office action in view of this response and to allow all of the claims, claims 1-21, in the present application.

Applicants acknowledge the Examiner's remarks that claims 3-13 and 21 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1-2 and 14-20 and 22-28 are rejected under 35 USC 103(a) as being unpatentable over Hauske et al (US Patent No 4,512,982) in view of Yang (US Patent No

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5,441,939) for the reasons set forth in the Office Action of June 13, 2000. The Examiner states the compounds disclosed by Yang are closely analogous erythromycin derivatives having antibacterial activity. A person of ordinary skill in the art at the time the instant invention was made would have expected that by modifying erythromycin derivatives disclosed by Hauske et al at the 4" position in accordance with the teaching of Yang would result in compounds having antibacterial activity. Note that Yang teaches an alkyl or alkenyl substituent at the 4"-position. Applicants respectfully traverse for the following reasons.

The compounds described by Hauske et al as possessing antibacterial activity include 9a-aza-9a homoerythromycin compounds having hydrogen or amino 4" substituents, provided these are always different, and further, compounds having an oxo group at the 4" position. The amino group may also be acylated (column 3, lines 4 to 15).

The compounds described by Yang et al as possessing antibacterial activity include 3"-desmethoxy erythromycin or azithromycin derivatives having as its 4" substituents, either a hydroxy and an alkyl, alkenyl or phenyl group, or a hydrogen and a specified amino derivative (column 2 lines 40 to 65).

As described in the affidavit submitted pursuant to 35 USC 1.132, enclosed herewith, the compounds of the present invention surprisingly provide substantially greater *in vivo* antibacterial activity based on mouse PD50 data when compared to a compound having the ring structure of Hauske with a 4" substituent described by Yang et al. This was not suggested by the cited references and would not have been obvious or reasonably expected based on Hauske or Yang et al, either alone or taken in combination. As described in the affidavit, it would not be reasonable to expect, based on the descriptions of Yang et al and Hauske, that all or any of the Yang et al substituents would, if substituted into the ring structure described Hauske be expected to show antibacterial activity. Based on the data presented in the affidavit, Applicants submit it was unpredictable at the time of the present invention as to which, if any, of the 4" substituents described by Yang et al, i.e., alkyl, alkenyl or phenyl group, or a hydrogen and a specified amino derivative (column 2 lines 40 to 65 of Yang et al) would, if substituted into the ring structure described by Hauske, provide for compounds exhibiting antibacterial activity. The rejection under 35 USC 103(a) should therefore be withdrawn.

Furthermore, Applicants respectfully submit the claims of the present invention are unobvious in view of their remarks made in the paper dated December 11, 2000 in response to the first Office action dated June 13, 2000. These remarks are summarized below.

One of ordinary skill in the art would not reasonably expect that substitution of the 4" substituents described by Yang et al in the ring structure described by Hauske et al would exhibit superior antibacterial activity since the compounds described by Yang et al have an entirely different ring structure from the compounds of the present invention. It would not be obvious, just because the 4" substituents when present in the ring structure described by Yang et al are described as antibacterially active, would when present in the significantly different ring structure of Hauske et al, provide for compounds that possess antibacterial activity. This supported by the affidavit mentioned above and enclosed herewith.

The antibacterial compounds described by Yang et al have a CH_2 -$N(CH_3)$, $N(CH_3)$-CH_2, or O=C group present in the 8 position of its ring structure. The compounds of the present invention have only a hydrogen substituting the ring template (have an N-H group as part of its ring structure in the 9a position). In addition, a further significant difference is that the 3" substituent described by Yang et al is a monosubstituted methyl group, while the 3" position of the compounds of the present invention is di-substituted with a methoxy and methyl group. Yang et al do not mention or suggest those aspects of the described ring structure that results in antibacterial activity. Given the differences in ring structure from the present invention, it would not have been obvious that if one substituted the 4" substituents of Yang et al for the 4" substituents of Hauske, the resulting compounds would possess antibacterial activity.

Hauske et al do not mention or suggest the 4" substituents of the presently claimed compounds as providing for antibacterial activity in the compounds of the present invention, but rather, describe H and amino substituents or an oxo substituent as the substituents of its 4" ring structure. It would not have been obvious to substitute the claimed 4" substituents that include hydroxy alkyl, alkynyl, alkenyl, etc., substituents (see claims 1 to 28) and which differ structurally from those of Hauske et al, and therefore could not have been reasonably expected to possess antibacterial activity based on the 4" substituents described by Hauske et

al., with or without the description provided by Yang et al.

In view of the above remarks, Applicants earnestly believe the present application contains patentable subject matter and earnestly request reconsideration and allowance of claims 1-21, all of the claims in the present application.

Respectfully,

Date: June 7, 2001

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